REMARKS

Entry of this amendment is respectfully requested. No new matter is added by the amendment, because the amended application us fully supported by the specification as filed.

Claims 57 to 82 are in this application. Claims 1-56 having been canceled in this response.

The present claims are essentially those previously presented, but amendments have been made for completeness and clarity as the specific variables are explicitly recited, and the method claims have been added and supplemented so that the method claims now are all explicitly dependent on composition claims, and this is believed to make the relationship of the claims clearer. In particular, for Claim 57, the variables $R^{1(i)}$ to G^{13} find support on pages 8 – 24 in the specification as filed.

Claim 57 to 68 are directed to pharmaceutical compositions, Claim 69-71 are directed to formulations of the compositions, and Claims 72-82 are method of use claims.

The following table shows the relationship between the new claims and the previous claims.

New Claim	Previous Claim	Comments
57	55 and 56	Pharmaceutical compositions of formula (I)
58	49	Pharmaceutical compositions of Claim 57
59	42	Pharmaceutical compositions of Claim 57
60	43	Pharmaceutical compositions of Claim 57
61	44	Pharmaceutical compositions of Claim 57
62	45	Pharmaceutical compositions of Claim 57
63	46	Pharmaceutical compositions of Claim 57
64	47	Pharmaceutical compositions of Claim 63
65	48	Pharmaceutical compositions of Claim 57
66	51	Pharmaceutical compositions of formula (I)
67	52	Pharmaceutical compositions of Claim 66
68	41	Pharmaceutical compositions of formula (I)

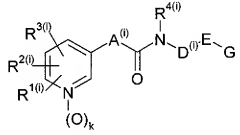
New Claim	Previous Claim	Comments
69	--	Formulations of compositions of Claim 57
70	--	Formulations of Claim 57
71	--	Formulations of Claim 57
72	32	Method for reducing or neutralizing side effects ...
73	33	Method of Claim 72
74	34	Method of Claim 73
75	35	Method of Claim 74
76	36	Method of Claim 75
77	37	Method of Claim 73
78	38	Method of Claim 72
79	39	Method of Claim 71
80	40	Method of Claim 73
81	50	Method of Claim 72
82	40	Method of Claim 72

Applicants note that both the compound having vitamin PP activity and the compound of formula I are defined by Markush groups, in method Claims 73 and 68 (formerly Claims 33 and 41) for the compound having vitamin PP activity, and in Claims 78 and 68 (formerly Claims 38 and 41) for the compound of formula I. Accordingly, the new and amended claim set constitutes a single invention.

And as set forth in MPEP 803.02, second paragraph, "unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

Applicants further note that the compounds having vitamin PP activity clearly share a common utility (the vitamin PP activity itself), and share a substantial common feature disclosed as being essential to that activity (all the compounds are based on 3-pyridylmethanols, 3-pyridylcarboxylates [nicotinic acids], or 3-pyridylcarboxamides [nicotinamides], and their derivatives. The compounds of formula I also share a common activity (they are disclosed as cancerostatic or immunosuppressive agents), and share a

substantial common feature disclosed as being essential to that activity (all the compounds are of the formula



(I)

as defined in Claims 78 and 68 (formerly Claims 38 and 41).

Rejection under 35 U.S.C. § 112, Second Paragraph

On page 2 of the Office Action mailed June 28, 2006, the Examiner maintained the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention with respect to the recitation "or a prodrug thereof" in Claims 72, 73, 75, 76 and 57 (formerly Claims 32, 33, 35, 36 and 56). The Examiner suggested that where those esters are considered by Applicants to be prodrugs, the corresponding esters should be recited in the claims. As amended, the phrase "or a prodrug thereof" recited in all amended claims has been replaced by the phrase "or an ester thereof."

Withdrawal of the 35 U.S.C. § 112, second paragraph is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

On page 3 of the Office Action, the Examiner maintained the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. § 102(b) as being anticipated by Nurmukhembetov et al (*Kardiologia* abstract). According to the Examiner's rejection, "Nurmukhembetov teaches the administration of the compound niacinamide having PP vitamin activity to reduce side effects relating to cardiac contractility as a result of an injection of the cancerostatic agent adriblastin."

Applicants respectfully traverse the rejection as it applies to Claims 72-76 and 57 (formerly Claims 32-36 and 55) over Nurmukhembetov *et al.*

To anticipate a claim, the reference must teach every element of the claim. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the ... claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

As summarized in the abstract of Nurmukhembetov, Nurmukhembetov simply discloses the pretreatment of nicotinamide 3 days prior to intraperitoneal injection of adriblastin for the prevention of cardiac contractility in adriblastin-treated rats. Applicants respectfully assert that Nurmukhembetov does not disclose nor suggest the subject matter of independent Claim 72 (formerly Claim 32) of the present application, which is a method for reducing side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent by the prophylactic or therapeutic administration of a compound having vitamin PP activity or an ester thereof.

Applicants submit that it is abundantly clear that a method for the prevention of cardiac contractility in adriblastin-treated rats does not anticipate nor suggest the method for reducing side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent as recited in Claim 72 (formerly Claim 32) of the present application, because Nurmukhembetov does not teach every element of Claim 72.

Withdrawal of the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. 102(b) over Nurmukhembetov *et al* is respectfully requested.

On pages 3-4 of the Office action, the Examiner maintained the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. 102(b) over Giri *et al.*, (*Advances in experimental medicine and biology*). According to the Examiner, Giri *et al* teaches the administration of the compound niacin having PP vitamin activity "to reduce the chemically-induced side effect interstitial pulmonary fibrosis that results from administration of the cancerostatic agent bleomycin."

Applicants respectfully disagree with the Examiner's characterization of the disclosure of Giri *et al* and the conclusion drawn therefrom, as it relates to the amended Claim 72 of the present invention. Giri *et al* teach that the combined treatment with taurine in drinking water and niacin IP daily significantly decreased the BO-induced increases in lung MDAE and calcium content etc ... and completely ameliorated the BL-induced increases in the lung collagen accumulation. Applicants respectfully assert that Giri *et al* teach the administration of a combination of products including the compound taurine, and do not teach nor even suggest the method for reducing side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent comprising administering a compound having vitamin PP activity or an ester thereof, as recited in Claim 72 (formerly Claim 32) of the present application.

Because Giri *et al* do not teach or even suggest each and every element of Claim 72 (formerly Claim 32) of the present application, Giri *et al* do not anticipate Claim 72 of the present application. Withdrawal of the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. 102(b) over Giri *et al.* is respectfully requested.

On pages 4-5 of the Office Action, the Examiner maintained the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. 102(b) over Stevens *et al.*, (*British Journal of Dermatology*). According to the Examiner, "Stevens teaches the administration of the compound having PP vitamin activity, nicotinic acid, to neutralize a dermatologic side effect, a rash, that was exacerbated by administration of the cancerostatic agent 5-fluorouracil. Pellagra is presented as a chemically-induced side effect secondary to 5-fluorouracil."

Applicants respectfully disagree with the Examiner's characterization of Stevens *et al* as a disclosure that is even remotely related to the claims of the present application. Stevens *et al* offers the observations that "the typical changes of pellagra ... rash and an associated acute deterioration in cerebral function were exacerbated by treatment with 5-fluorouracil" and "reasons for possible under diagnosis of pellagra in association with malignant disease" and that "[t]he importance of considering nicotinic-acid deficiency in patients with malignant disease has not been emphasized in the literature." (Underline added).

Accordingly, Stevens *et al* do not teach nor even suggest the method for reducing side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent comprising administering a compound having vitamin PP activity or an ester thereof, as recited in Claim 72 (formerly Claim 32) of the present application.

Withdrawal of the rejection of Claims 72-76 and 57 (formerly Claims 32-36 and 55) under 35 U.S.C. 102(b) over Stevens *et al* is respectfully requested.

Claims 57 to 82 pending in this application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Allowance of the Claims 57 to 82 is respectfully requested.

Kindly direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: October 25, 2006

Sam L. Nguyen
Attorney for Applicants
Reg. No. 52,496

Customer No.: 25213
Heller Ehrman LLP
275 Middlefield Road
Menlo Park, CA 94025-3506
Direct: 650.324.7028
Main: 650.324.7000

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